Principles of Electronic Nanobiosensors

Unit 3: Sensitivity
Lecture 3.1: Nanobiosensors:
   Sensitivity and Types of Biosensors

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Outline

• Background and introduction
  – Geometry of diffusion defines the detection limits
  – Sensor must be sensitive to the analyte

• Three types of nanobiosensors
  – Tags vs. transducers

• Potentiometric sensor
  – Basic operation
  – Puzzle regarding analyte density

• Conclusions
The importance of sensitivity

If the sensor does not notice the analyte, it does not exist!
Part 1: Geometry of diffusion

Regardless the sensors, the diffusion limits must be obeyed.
Sensitivity defined by detection mechanism

Si NW biosensor

Capture Probe

Response vs. Time

\[ t_s \text{ response time}, \Delta G, G_0 \]

Limits of detection

\[ \rho_0 : N_s \times t_s \left( \frac{3-D_F}{2} \right) \]

Minimum # molecules

Diffusion geometry
Types of sensors: tags vs. transducer

- Charge
- Mass
- Electron affinity
- Optical/Magnetic tag
- MOSFET current
- Frequency of cantilevers
- GMR/Spin Valve current
- SPR resonance
Three types of sensors

Potentiometric

Amperometric

Cantilever

- **Potentiometric**: Fluid Gate
  - Charge to current

- **Amperometric**: Ref. & Aux. Electrode
  - Chemical to current

- **Cantilever**: Gate
  - Mass to frequency

References:
- Alam, Principles of Nanobiosensors, 2013
A short history of Potentiometric sensors

Virus/bacteria → Protein/DNA → PCR

pH-meter (potentiometric) → Glucose (amperometric) → Genome sequencer

Vacuum tube → MOS → IC

Important as pH-meter and genome sequencers
Transistor physics (potentiometric sensor)

\[ I = q \times n \times \nu \times A \]

\[ \nu = \mu E = \mu \frac{V_D}{L} \]
Sensitivity of a MOSFET-based potentiometric sensor

\[ S \equiv \frac{I_{D,\text{after}} - I_{D,\text{before}}}{I_{D,\text{before}}} \equiv \frac{\Delta I_D}{I_D} \]

Alam, Principles of Nanobiosensors, 2013
How does a potentiometric Field Effect Transistor work (accumulation)

\[ Q_{bio} = Q_{MOS} = C_0 \phi \]

\[ I = Q_{MOS} \nu = Q_{bio} \frac{\mu V_D}{L} \]

Change in current proportional to the total charge

Alam, Principles of Nanobiosensors, 2013
Recall from Lecture 3: Sensitivity Gain

\[ I_b = q N_D \times \pi R_b^2 \times \nu \]
\[ I_a = q N_D \times \pi R_a^2 \times \nu \]
\[ Q_{bio} = 2\pi R \times q N_{bio} \]
\[ = q N_D (\pi R_b^2 - \pi R_a^2) \]
\[ S \equiv \frac{I_a - I_b}{I_b} \]
\[ S \sim \frac{2 N_{bio}}{N_D R} \]
Concentration dependence

\[ \frac{dN}{dt} = k_F(N_0 - N)\rho_0 - k_R N \]

\[ N_{bio} = \frac{k_F N_0 \rho_0}{k_F N_0 \rho + k_R} \propto \rho_0 \]

\[ Q_{bio} \propto \rho_0 \]

\[ I = Q_{bio} \frac{\mu V_D}{L} \propto \rho_0 \]

A linear response is expected
Puzzle of Concentration dependence

Optical response

Potentiometric Response

Much weaker and completely wrong dependence!
Evolution of a MOSFET

Gate metal

oxide

substrate

Ref. electrode

fluid

Distributed analyte

Analyte is charged

Need salt too!

I_D

I_D

Alam, Principles of Nanobiosensors, 2013
DNA binding and Salt screening

Alam, Principles of Nanobiosensors, 2013
The classical theory does not work ...

\[ S = 2N_{bio}/RN_D \propto \left( \frac{2}{qRN_D} \right) \times \rho_0 \]

- Theory predicts linear response, experiments show strong sub-linear response.
- Theory shows no dependence on salt concentration, pH, etc. and yet experiments show strong dependence.
- There is no notion of time and yet experiments show strong time dependence.

\[ S(t) \sim c_1 \left[ \ln(\rho_0) + \frac{(3 - D_F)\ln(t)}{2} - \frac{\ln(I_0)}{2} + \alpha[pH] \right] + c_3 \]

Alam, Principles of Nanobiosensors, 2013
Conclusions

• Two things define sensor sensitivity of a sensor: geometry of diffusion and transduction mechanism.

• Geometry of diffusion defines the ultimate limit, while geometry and transduction together define sensor-specific limits.

• Potentiometric, amperometric, and mass-sensors have long history. There are unique challenges of reducing the sensor dimensions to nanoscale.

• Classical theory of potentiometric sensor cannot account for many features observed experimentally.
Review Questions

• Why is sensitivity defined as a ratio of quantities before and after capture? Shouldn’t the absolute value be more relevant? (Hint: Think noise)
• What was the original use of potentiometric sensors?
• Why is tagging important?
• Give an example of amperometric sensor in wide use and can be purchased in any supermarket.